UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/288,326	04/08/99	SACHS G	17282

HM12/0426

ALLERGAN INC
2525 DUPONT DRIVE
IRVINE CA 92612

EXAMINER	
CLEMENS,K	
ART UNIT	**PAPER NUMBER**
1644	7

DATE MAILED: 04/26/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/288,326	Sachs et al.
Examiner	**Group Art Unit**
Karen Clemens	1644

☒ Responsive to communication(s) filed on Mar 14, 2000 and Sept. 3, 1999.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-24 is/are pending in the application.

Of the above, claim(s) 9-12 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-8 and 13-24 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1644, Group 1640, Technology Center 1600.

DETAILED ACTION

Claims 1-24 are pending.

Applicant's election with traverse of Group I, claims 1-24, and election of the following species: 1) a specific binding element comprising SEQ ID NO:6; 2) a specific translocation element comprising the N-terminal half of the heavy chain of a *Clostridium botulinum* neurotoxin; 3) a specific therapeutic element cleaving a SNARE protein comprising the light chain of BoNT/A or E, cleaving SNAP-25; and 4) a specific spacer moiety comprising a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region such as SEQ ID NO:11, in Paper No. 6 is acknowledged.

The traversal is on the grounds that the Examiner's search of the different binding element species (SEQ ID NO:2- 6) is not deemed burdensome as they are all subsets of SEQ ID NO:2 and all contain the biologically active C-terminal peptide. This is not found persuasive because although related, the peptides are comprised of different amino acid sequences and although the peptides all contain the bioactive C-terminal peptide, the biological activity of the peptides can differ. For example, Kreis et al. demonstrate a difference in the ability of CCK-58 (SEQ ID NO:2) and CCK-8 (SEQ ID NO:6) to stimulate afferent nerve discharge (*Neuroscience Letters* 230(2):89-92). Therefore, a search of one is not co-extensive with a search of the other and they are therefore distinct.

The requirement is still deemed proper is therefore made final.

Claims 1-8 and 13-24 read on the elected species and are under examination. Claims 9-12 (non-elected species of Group I) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention.

Non-elected Claims 25-40 in Group II have been canceled.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of *35 U.S.C. § 103* which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that

the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under *subsection (f) or (g)* of *section 102* of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

A) Claims 1-8 and 13, 17, and 21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Foster et al. (WO 9633273, 1996) in view of Gaisano et al. (*J. Biol. Chem.* 269(25):17062-17066, 1994) and Scheele et al. (*Gatroenterology* 92(2):345-353, 1987).

Foster et al. teach a composition comprising a binding element to a neuronal cell surface marker (see page 9, lines 19-21 and page 12, line 25 to page 13, line 6, in particular), a translocation element consisting of the N-terminal half of a the heavy chain of a clostridial neurotoxin (*C. botulinum* or *C. tetani*; see page 9, lines 8-12 and page 12, lines 1-24 in particular) a therapeutic element consisting of the light chain of a clostridial neurotoxin (*C. botulinum* or *C. tetani*) capable of cleaving the SNARE protein, synaptobrevin, syntaxin or SNAP-25 (see page 12, lines 13-19 in particular) which will inhibit vesicle exocytosis and secretion, and a spacer moiety separating the binding element and the translocation element (see page 13, lines 18-24 in particular).

However, Foster et al. do not teach a composition which inhibits enzyme secretion from a pancreatic acinar cell for use in the treatment of acute pancreatitis. Foster et al. also do not teach targeting the CCK-A receptor on pancreatic acinar cells using the secretagogue CCK-8 (SEQ ID NO:6) as the binding element.

However, Gaisano et al. teach the inhibition of enzyme secretion in a pancreatic acinar cell by treatment of the cells with a clostridial neurotoxin which cleaves a SNARE protein (see page 17062 to 17063, the introduction in particular) preventing zymogen granule exocytosis and enzyme secretion from pancreatic acinar cells. Further, Scheele et al. teach that pancreatic cells

release enzymes by zymogen granule exocytosis in response to physiological concentrations of such secretagogues as cholecystokinin (CCK) and the release of these pancreatic enzymes result in serious pathologic sequelae such as acute pancreatitis with pancreatic edema, inflammation and necrosis (see page 345 and page 353 in particular). It is known in the art at the time the invention was made that CCK-8 binds to CCK-A receptors on pancreatic acinar cells with high affinity (see Pohl et al., page 18180, introduction in particular; Form 1449).

Therefore, it would be been obvious to one having ordinary skill in the art at the time the invention was made to design a composition consisting of a binding element, a translocation element, a therapeutic element and a spacer moiety as taught by Foster et al. which inhibits enzyme secretion from pancreatic acinar cells as taught by Gaisano et al. using the secretagogue, cholecystokinin (CCK of which the bioactive form is CCK 8) as taught by Scheele et al. which binds to CCK-A pancreatic receptors as taught by Pohl et al. One having ordinary skill in the art at the time the invention was made would have been motivated to use this composition to inhibit enzyme secretion from the pancreas by blocking enzyme exocytosis which is associated with serious pathologic sequelae such as acute pancreatitis as taught by Scheele.

B) Claims 14-16, 18-20, and 22-24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Foster et al., Gaisano et al. and Scheele et al. as applied to claims 1-8, 13, 17, and 21 and further in view of Dangl et al. (*EMBO J.* 7(7):1989-94, 1988).

Foster et al., Gaisano et al. and Scheele et al. have been discussed supra.

The claimed invention further differs from the combined reference teachings only by the recitation that the spacer moiety comprises a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region (such as SEQ ID. NO:11).

However, Dangl et al., teach that the immunoglobulin hinge region (SEQ ID NO:11) allows for flexible movement of the antigen binding regions of the immunoglobulin molecule such that two antigen binding sites can move relative to each other to bind determinants separated by different distances and orientations (see page 1991, Table 1 in particular). Dangl et al. further teach that this hinge region may function as a spacer, facilitating a proper spacial relationship between the Fab and Fc regions, allowing for both antigen binding and Fc effector functions such as complement activation (see page 1989, introduction, and page 1991, Table 1 in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to design a composition with a spacer moiety separating the translocation and binding element as taught by Foster et al. in which the spacer moiety comprises an immunoglobulin hinge region as taught by Dangl et al. One having ordinary skill in the art at the time the invention was made would have been motivated to use an immunoglobulin hinge region

as a spacer moiety since the hinge region allows for a high degree of flexibility in the movement of the domains, such as the translocation and binding elements, which it interconnects.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Clemens whose telephone number is (703) 308-8365. The examiner can normally be reached Monday through Friday from 8:00 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Karen Clemens, Ph.D.
Patent Examiner
Technology Center 1600
April 24, 2000

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP 1800 1640